

Research Article

Spectrum of lymph node lesions on cytology in rural Haryana: a retrospective analysis

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ABSTRACT

Background: Fine Needle Aspiration Cytology (FNAC) is a simple, rapid, cost effective and reliable technique which can be used as a routine outpatient department (OPD) procedure and first line of investigation in diagnosing a variety of superficial and deep lesions. Lymphadenopathy is of great clinical significance and the underlying cause may range from a treatable infectious etiology to malignant neoplasms. In this study, we describe the diagnostic utility of FNAC in the assessment of lymph node lesions with an emphasis on the diagnosis of non-neoplastic, benign and malignant neoplastic processes. Cytomorphological patterns of tuberculous lymphadenitis were also observed.

Methods: This was a retrospective study and a total of 736 patients including all age groups and both sexes presenting with palpable or deep lymph nodes in FNAC clinic of our institute over a period of 2 years were included in our study. FNAC was conducted with 22-24 Gauge disposable needles attached to 20c.c syringes. Smears were fixed in 95% ethyl alcohol and stained with Papanicolaou stain. Leishman stain was done on air dried smears. Ziehl-Neelsen (ZN) staining was done wherever required.

Results: Out of 736 aspirations from lymph nodes, the most frequent cause of lymphadenopathy was found to be Tuberculosis with 419 cases (56.92%). The next frequent diagnosis was reactive lymphadenitis with 193 cases (26.22%) followed by metastatic lymphadenopathy in 47 cases (6.38%). A diagnosis of lymphoproliferative disorder was rendered in 20 cases (2.71%). In 10 cases (1.35%) FNAC was inconclusive.

Conclusion: In our study, the predominant cause of lymphadenopathy was tuberculous lymphadenitis, seen in more than half of total cases, followed by reactive lymphadenopathy and malignant neoplasms. FNAC was helpful in establishing the diagnosis in 98.65% of the cases.

Keywords: FNAC, Lymphadenopathy, Tuberculous lymphadenitis, Metastatic lymphadenitis

INTRODUCTION

Lymphadenopathy refers to the nodes which are abnormal in size, consistency and number.¹ It is one of the commonest clinical presentations of patients attending the Out Patient Department. The degree and pattern of morphological changes are dependent on the inciting stimulus and the intensity of the response. Thus,

lymphadenopathy may be an incidental finding and/ or primary or secondary manifestation of underlying diseases which may be neoplastic or non- neoplastic.² FNAC as first line of investigation has assumed importance in diagnosing a variety of disease processes as it is rapid, simple, reliable, minimally invasive and cost effective procedure which can be used in outpatient setting.³ FNAC has an important role in the evaluation of

peripheral lymphadenopathy and it can be used as a safe alternative to excision biopsy.⁴ In developing countries, almost two third of the cases are due to tuberculosis. Tuberculous lymphadenopathy is the commonest form of extrapulmonary tuberculosis.⁵ Our experience of the diagnostic utility of FNAC in the assessment of lymphadenopathy is presented. The study highlights the epidemiological patterns and cytomorphological spectrum of lymph node lesions in this rural region with emphasis on cytological spectrum in diagnosis of pattern of tuberculosis; also providing details about burden of disease in this region.

METHODS

This study was a retrospective review of FNAC of lymph node lesions between Oct 2012 and Sept 2014. Data was retrieved from the records of the Department of Pathology, SHKM GMC, Nalhar, Mewat, Haryana, India. FNAC was performed on 736 cases of palpable and /deep lymphadenopathy. A brief clinical history followed by meticulous physical examination was done and the findings were noted. FNAC was performed using 22-24 Gauge needles attached to 20 ml syringes. One to two passes were given and the aspirated material was smeared onto glass slides. Smears were fixed in 95% ethyl alcohol and stained with Papanicolaou stain. Leishman stain was done on air dried smears. Ziehl- Neelsen (ZN) staining was done whenever a cytological diagnosis of granulomatous disease was made and also in cases with abundant necrosis and suppuration. In cases where fluid was aspirated on FNAC, the fluid was centrifuged and smears were made from the sediment followed by the above staining methods. The cytological diagnosis for each case was based on cytomorphology and available clinical information. The diagnoses were categorized broadly as tuberculous lymphadenitis, Reactive lymphadenitis, acute suppurative lymphadenopathy metastatic lymphadenopathy and lymphomas. The tuberculous lymphadenitis cases were further divided into three groups on the basis of cytomorphological analysis: group 1 - Granulomas without necrosis, group 2 - Caseating epithelioid granuloma and group 3 - Necrotizing lymphadenitis. In those cases where lymphoma or leukemic infiltration of lymph nodes was suspected on cytology, bone marrow aspiration and other necessary haematological investigations were done. Data was entered in excel spread sheet and statistical analysis was done using epidemiological information package. Kruskal-Wallis's Chi square test was used. P value <0.05 was taken to represent significant difference.

RESULTS

A total of 736 FNACs were studied and the ages of the patients ranged from 21days to 80 years with the male to female ratio of 0.87:1. The youngest patient had acute suppurative lymphadenopathy whereas the oldest patient had Non-Hodgkin's lymphoma. Cervical lymph nodes were enlarged in 630 of 736 cases (85.59%) followed by

axillary lymph nodes in 59 cases (8.01%), inguinal lymph nodes in 21 cases (2.85%) , supraclavicular lymphnodes in 19 cases (2.58%), in one case each (0.13%) the site of lymphadenopathy was arm and mesenteric lymphnodes. Multiple sites were involved in 5 cases (0.67%) (Table 1). The size of the lymph nodes varied from 0.5cm to 5cm. The lymph nodes in tuberculosis were multiple, soft to firm and matted; while they were discrete in reactive lymphadenitis and firm to hard and fixed in majority of metastatic lesions. Tuberculous lymphadenitis was the most frequent diagnosis with 419 cases (56.92%) (Table 2). Out of 736 cases, maximum number of cases were recorded in the age group 10-19 years (Table 3). The tuberculous lymphadenitis cases were further divided into three groups on the basis of cytomorphological analysis; group1: Granulomas without necrosis - 113/419 (26.96%), group 2: Caseating epithelioid granuloma - 288/419 (68.97%) (Figure 1a & 1b) and group 3: Necrotizing lymphadenitis - 18/419 (4.29%). Acid fast bacilli positivity on ZN staining was seen in 95 out of 419 cases (22.67%) of tuberculous lymphadenitis. Next frequent diagnosis was reactive lymphadenitis with 193 out of 736 cases (26.22%). Malignant lymph node lesions were seen in 68 out of 736 cases (9.24%). These comprised of metastatic lymphadenopathy 47/736 (6.38%), malignant lymphomas 20/736 (2.71%) and one case of myeloproliferative lesion in lymph node 1/736 (0.135%). The metastatic lesions were Squamous cell carcinoma in 42.55% (20/47) cases (Figure 2a & 2b), poorly differentiated carcinoma in 36.17% (17/47) cases, adenocarcinoma in 8.51% (4/47) cases, papillary carcinoma thyroid in 8.51% (4/47) cases and carcinoma breast in 4.25% (2/47) cases. Metastatic lesions were more common in cervical lymph nodes (Table 4). Out of 20 cases of lymphoma, 17 were Non- Hodgkin's lymphoma and 3 were Hodgkin's lymphoma. Acute suppurative lymphadenopathy was seen in 45 out of 736 cases (6.11%). One case of lymphangioma was also reported. In 10 cases, the aspirate was inadequate for a definite diagnosis (1.35%).

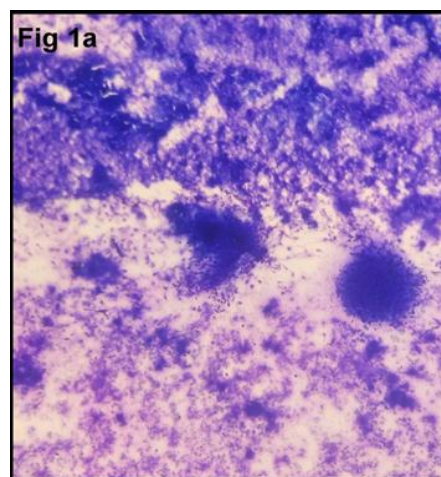


Figure 1a: Smear shows epithelioid cell granulomas along with caseous necrosis in background (Leishman stain; x100).

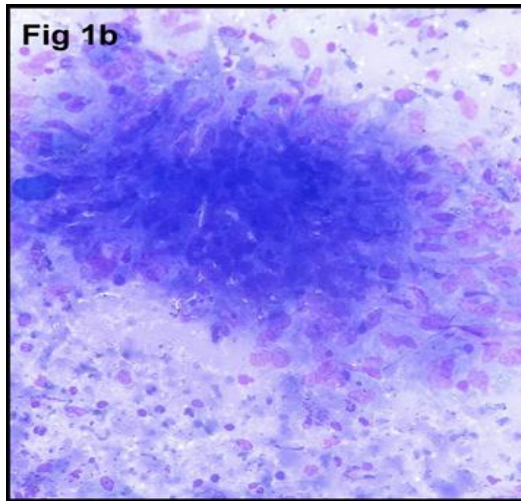


Figure 1b: Smear shows caseating epithelioid cell granulomas and inflammatory cells in background (Leishman stain; x400).

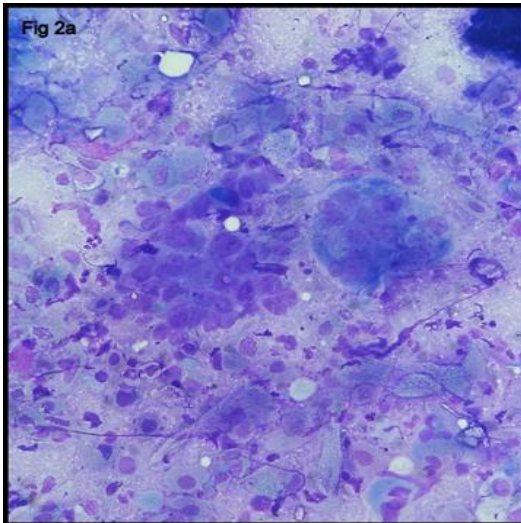


Figure 2a: Smear shows clusters of atypical epithelial cells with prominent nucleoli and dense basophilic cytoplasm (Leishman stain; x400).

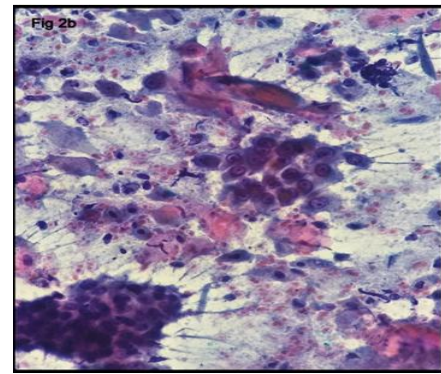


Figure 2b: Smear shows clusters of atypical epithelial cells with prominent nucleoli and orangeophilic cytoplasm (Pap stain; x400).

Table 1: Sites of lymphnode involvement (n=736).

Sites of lymphnode involvement (n=736)	
Cervical	630
Axillary	59
Supraclavicular	19
Inguinal	21
Mesenteric	1
Extremities	1
Multiple	5

Table 2: Cytological diagnosis of 736 cases.

Cytological diagnosis	Number of cases	Percentage
Tuberculous lymphadenitis	419	56.93
Reactive lymphadenitis	193	26.22
Acute suppurative lymphadenitis	45	6.11
Metastatic lymphadenopathy	47	6.38
Malignant lymphoma	20	2.72
Myeloproliferative disorder	1	0.14
Lymphangioma	1	0.14
Inadequate	10	1.36

Table 3: Age and sex distribution of patients of lymphadenopathy.

Age group (years)	Tuberculous lymphadenitis		Reactive		Acute suppurative lymphadenitis		Metastatic lymphadenopathy		Malignant lymphoma		Others		Inadequate	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F
0-9	27	25	48	14	5	5	0	0	1	0	0	0	1	0
10-19	48	87	48	37	6	12	0	0	1	1	0	1	0	4
20-29	57	73	6	18	1	3	1	3	1	2	0	0	1	3
30-39	17	37	3	7	2	2	5	5	2	0	0	0	0	0
40-49	10	16	5	6	1	2	4	0	2	1	0	1	0	0
50-59	6	5	1	0	1	1	10	1	2	1	0	0	1	0
60-69	3	5	0	0	1	3	12	1	1	0	0	0	0	0
70-79	2	0	0	0	0	0	2	3	2	2	0	0	0	0
80-89	0	1	0	0	0	0	0	0	1	0	0	0	0	0

Table 4: Lymphnode groups involved in various lymph node lesions.

Site	Tuberculous lymphadenitis	Reactive lymphadenitis	Acute suppurative lymphadenitis	Metastatic lymphadenopathy	Malignant lymphoma	Others	Inadequate
Cervical	364	173	32	44	8	2	7
Axillary	36	7	8	1	5	0	2
Supraclavicular	9	5	3	1	0	0	1
Inguinal	10	6	2	1	2	0	0
Mesenteric	0	0	0	0	1	0	0
Extremities	0	1	0	0	0	0	0
Multiple	0	1	0	0	4	0	0
Total	419	193	45	47	20	2	10

Table 5: Age distribution of patients of lymphadenopathy.

Age group (years)	Tuberculous lymphadenitis	Reactive lymphadenitis	Acute suppurative lymphadenitis	Metastatic lymphadenopathy	Malignant lymphoma	Others	Inadequate
	P value	P value	P value	P value	P value	P value	P value
0-9	0.074	0.0001	0.29	#	#		
10-19	0.14	0.79	0.61	#	0.58		
20-29	0.36	0.0001	0.51	0.05	0.27		
30-39	0.14	0.07	0.48	0.086	#		
40-49	0.82	0.4	0.68	0.26	0.7	#	#
50-59	0.33	#	0.61	0.11	0.7		
60-69	0.85	#	0.51	0.05	#		
70-79	0.16	#	#	0.12	0.43		
80-89	#	#	#	#	#		

#P value was not calculated because of insufficient number in the cells.

DISCUSSION

FNAC is an important diagnostic tool to aid in the diagnosis of lymph node lesions. It is inexpensive, safe and quick and reduces the need for surgical biopsy.⁶ Aspiration of lymph nodes was first done by Griey and Gray in 1904, in a patient with sleeping sickness⁷. It was Dudgeon and Patrick in 1927, who first used FNAC in diagnosing tuberculous lymphadenitis.⁸ In the present study, an attempt has been made to study the cytomorphological spectrum and epidemiological pattern of lymph node lesions. In this study, maximum number of cases were recorded in the age group 10-19 years. While the maximum number of cases in other studies were recorded in age group 21-30 years.^{3,9-12} Cervical lymph nodes were the most common group of lymph nodes involved, which is similar to that observed by Pavithra et al.³, Chandanwale et al.,¹² Kochhar et al.¹³ and Mohanty et al.¹⁴. Tuberculous lymphadenitis was the most common lesion and was reported in 56.92% cases and maximum number of these cases were in the age group 10-19 years with a female preponderance (M:F = 0.55:1) followed by 20-29 years and 0-9 years. The difference was found to be statistically significant (Table 5). A

declining trend was noted in incidence of tubercular lymphadenitis after 30 years of age, which was in concordance with that observed by Ahmed et al.¹⁵. It may be due to the development of immunity in older patients. The female preponderance of tuberculous lymphadenitis has been observed by Pavithra et al.,³ Fatima et al.⁶ and Chand et al.¹⁶. This may be because of malnutrition and overall low living standards among females in this area. Cervical lymph nodes (86.87%) were more commonly involved by tuberculosis, followed by axillary group (8.5%) in our study (Table 4). Similar observations were made by Pavithra et al.,³ Chand et al.¹⁶ and Khajuria et al.¹⁷ and Das et al.¹⁸ ZN staining for acid fast bacilli was seen in 22.67% cases in our study, while Chand et al.¹⁶ reported 44.54% cases, Bezabih et al.¹⁹ reported 59.5% cases, Paliwal et al.²⁰ reported 71% cases. On the other hand, a very low positivity rate of AFB (19.6% cases) on Z.N Staining was reported by Aggarwal et al.²¹ in their study. Low incidence of AFB positivity in our study may be due to combined maximum percentage (95.7%) of cases having epithelioid cell granulomas with necrosis and cases with epithelioid cell granulomas without necrosis unlike series of Paliwal et al.²⁰ where these groups together accounted for only 30.7%. In our study,

necrosis alone was seen in 18 cases and all of these were positive for acid fast bacilli. It has been observed that the foci of necrosis are associated with marked proliferation of tubercle bacilli whereas lymphocytes, epithelioid cells and multinucleated giant cells have a role in limiting the proliferation of AFB.^{18,22} Therefore, it is expected that FNAC from a tuberculous abscess yields more AFBs than early tuberculous lymphnodes.²³ The characteristic necrotic background comprising of eosinophilic granular material containing nuclear debris was described as 'tubercular diathesis'. Those cases lacking the typical finding and showing scattered epithelioid cells with or without granulomas or only necrotic material with neutrophilic infiltration were diagnosed as tuberculous lymphadenitis when this tubercular diathesis was found cytologically, even though AFB were absent in these smears.²⁴ Granulomas can be seen in a variety of other conditions causing lymphadenopathy including sarcoidosis, carcinoma, lymphoma, fungal diseases, cat scratch disease, collagen vascular disease and disease of the reticuloendothelial system.²⁵ But, in a region where tuberculous infection is common and other granulomatous diseases are rare, the presence of a granulomatous feature in FNAC is highly suggestive of tuberculosis.²³ In our study, the commonest cause of lymphadenopathy in pediatric age group males was reactive lymphadenitis whereas it was Tuberculous lymphadenitis in Pediatric age group females. This trend underscores the poor nutritional status of females in this region. Reactive lymphadenitis was seen in 26.22% cases which is comparable to study by Khan et al.²⁶ (28%). Whereas, in other studies reactive lymphadenitis was the most frequent diagnosis and its incidence ranged from 18.9% to 42%.^{13,14,17,27,28} Acute suppurative lymphadenopathy was observed in 6.11% cases in our study which is comparable with the study done by other workers, Patra et al.²⁹ (5.8%) and Kochhar et al. (4%).¹³ Lymph node aspirates in 6.38% cases showed metastatic deposits and males outnumbered females in these cases, (M: F= 2.6: 1). Maximum cases were seen in age groups 50-69 years and predominant deposits were of squamous cell carcinoma (42.55% of all metastatic lymph nodes). This correlates with findings of studies by Pavithra et al.³ (56.25%). The high incidence of squamous cell carcinoma may be due to the high incidence of smoking and tobacco chewing in this area. Malignant lymphoma constituted 2.72% of all cases in our study, which is comparable with the observations made by Fatima et al.⁶ (5.2%), and Hirachand et al.²⁷ (6.1%). In the present study, Non-Hodgkin's Lymphoma (NHL) and Hodgkin's Lymphoma (HL) constituted 2.31% and 0.41% respectively. This is comparable to study by Bhaskaran et al.³⁰ in which NHL and HL constituted 2.23% and 0.74% respectively. Patra et al.²⁹ in his study reported NHL and HL as 4.8% and 1.01% respectively. However, Hafez et al.³¹ reported that cases suspicious for NHL were 32.5% and were the prominent cause of cervical lymphadenopathy. Aspirates were inconclusive in 1.35% cases due to unsatisfactory smears. The causes of

unsatisfactory smears were scant cellular yield or hemodiluted smears.

CONCLUSION

FNAC of lymph nodes is an excellent first line investigation to determine the nature of lesion. It is quick, safe, minimally invasive, reliable and is readily accepted by the patient. Our study highlighted the various cytomorphological patterns of lymphadenopathy and revealed a huge burden of tuberculous lymphadenitis in this region.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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